PREVALENCE OF METABOLIC SYNDROME IN OBESE CHILDREN

DISSERTATION SUBMITTED FOR

M.D DEGREE (PAEDIATRICS) BRANCH VII

INSTITUTE OF CHILD HEALTH

AND

HOSPITAL FOR CHILDREN

MADRAS MEDICAL COLLEGE

THE TAMILNADU Dr. M.G.R. MEDICAL UNIVERSITY

CHENNAI

APRIL 2011

CERTIFICATE

This is to certify that the dissertation titled, "Prevalence of metabolic syndrome in obese children" submitted by Dr. L.Suganya, to the Faculty of Paediatrics, The Tamilnadu Dr. M.G.R Medical University, Chennai, in partial fulfillment of the requirements for the award of M.D. Degree (Paediatrics) is a bonafide research work carried out by her under our direct supervision and guidance, during the academic year 2008-2011

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Members Present: Dr.R.Kulandai Kasthuri, Chairperson

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TITLE: "PREVALENCE OF METABOLIC SYNDROME IN OVERWEIGHT AND OBESE CHILDREN".

The Institutional Review Board is satisfied with the proposal submitted by you. Hence, the board is pleased to approve the study.

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To
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ACKNOWLEDGEMENT

I thank with deep sense of gratitude **Prof Dr.P.Ramachandran, M.D., Paed., D.N.B.Paed.,** Professor of Paediatrics, Director and Superintendent of Institute of Child Health and Hospital for Children, Egmore, Chennai for her kind support and guidance.

I thank my unit **Chief Retd Prof.R. Kandasamy** M.D., D.C.H., for his guidance and support in doing this work.

I thank my unit **Chief Prof.S.Sundarai,M.D.,D.C.H.,** and my unit Assistant Professors and my guide **Dr. C.V.Ravisekar, M.D., D.C.H., D.N.B., Dr. S. Lakshmi ,M.D., D.C.H., Dr.K. Kumarasamy, M.D., D.C.H.,D.N.B., and Dr. Ravishankar** MD., DCH., for their whole hearted support, guidance and help rendered to this work.

I express my sincere thanks to **Dr. Srinivasan, D.C.H,** Registrar, Institute of Child health and Hospital for Children**,** for his support and guidance.

I would fail on my part if I forget to thank all my patients and their caretakers for their co-operation, without which, this work would not have been possible.

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INTRODUCTION

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Childhood obesity

Childhood obesity is one of the most serious public health challenges of the 21st century. The problem is global and is steadily affecting many low and middle income countries, particularly in urban settings. The prevalence has increased at an alarming rate. Globally, in 2010 the number of overweight children under the age of five is estimated to be over 42 million. Close to 35 million of these are living in developing countries.

Overweight and obese children are likely to stay obese into adulthood and more likely to develop diseases like diabetes and cardiovascular diseases at a younger age, the risks depend partly on the age of onset and on the duration of obesity. Obese children and adolescents suffer from both short-term and long-term health consequences.

Consequences of an unhealthy lifestyle during childhood

The most significant health consequences of childhood overweight and obesity, that often do not become apparent until adulthood, include:

- cardiovascular diseases (mainly heart disease and stroke);
- diabetes;
- musculoskeletal disorders, especially osteoarthritis; and
- certain types of cancer (endometrial, breast and colon).

The fundamental cause of childhood overweight and obesity is an energy imbalance between calories consumed and calories spent.

Global increases in childhood overweight and obesity are attributable to a number of factors including:

- A global shift in the diet towards increased intake of energy-dense foods that are high in fat and sugars but low in vitamins, minerals and other healthy micronutrients;
- A trend towards decreased physical activity levels due to the increasing sedentary nature of many forms of recreation time, changing modes of transportation, and increasing urbanization.

Metabolic syndrome:

Metabolic syndrome is also known as **metabolic syndrome X**, **syndrome X**, **insulin resistance syndrome**, **Reaven's syndrome** is a combination of medical disorders that increase the risk of developing cardiovascular diseases and diabetes.

Although the pathophysiology of this syndrome is incompletely understood, insulin resistance and abdominal obesity are central to many of the metabolic perturbations. Based on existing estimates the metabolic syndrome affects- nearly 1/4th of the populations in developed countries (1). Prevalence of the metabolic syndrome is increasing in developing countries, including India (1, 2). The cluster of metabolic abnormalities comprising the metabolic syndrome is evident even in Asian Indian children and adolescents (3-5)

Insulin resistance and resulting hyperinsulinemia have been implicated in the development of glucose intolerance (and progression to type 2 diabetes), hypertriglyceridemia, hypertension, polycystic ovary syndrome, hypercoagulability and vascular inflammation, as well as the eventual development of atherosclerotic cardiovascular disease manifested as myocardial infarction, stroke and myriad end organ diseases. Conversely, treatment and consequent improvement of insulin resistance have been shown to result in better outcomes in virtually all of these conditions. The main features of metabolic syndrome include insulin resistance, hypertension, cholesterol abnormalities, and an increased risk for clotting. Patients are most often overweight or obese. Insulin resistance refers to the diminished ability of cells to respond to the

action of insulin in promoting the transport of glucose from blood into muscles and other tissues.

Metabolic syndrome increases the risk of type 2 diabetes (the common type of diabetes) anywhere from 9-30 times over the normal population. That's a huge increase. As to the risk of heart disease, studies vary, but the metabolic syndrome appears to increase the risk 2-4 times that of the normal population.

There are other concerns as well that should be mentioned. Metabolic syndrome is associated with fat accumulation in the liver (fatty liver), resulting in inflammation and the potential for cirrhosis. The kidneys can also be affected, as there is an association with microalbuminuria the leaking of protein into the urine, a subtle but clear indication of kidney damage.

Other problems associated with metabolic syndrome include obstructive sleep apnea, polycystic ovary syndrome, increased risk of dementia with aging, and cognitive decline in the elderly.

Criteria of metabolic syndrome in children and adolescents

Age 6 to <10 years

- Obesity 90th percentile as assessed by waist circumference
- Metabolic syndrome cannot be diagnosed, but further measurements should be made if family history of metabolic syndrome, type 2 diabetes mellitus, dyslipidaemia, cardiovascular disease, hypertension, or obesity
- IDF suggests that a strong message for weight reduction should be delivered for those with abdominal obesity

Age 10 to <16 years

- Obesity 90th percentile (or adult cut-off if lower) as assessed by waist circumference
- Triglycerides 1.7 mmol/L
- HDL-cholesterol <1.03 mmol/L
- Blood pressure 130 mm Hg systolic or ?85 mm Hg diastolic
- Glucose 5.6 mmol/L (oral glucose tolerance test recommended) or known type 2 diabetes mellitus

Age >16 years

Use existing IDF criteria for adults:

According to the new IDF definition, for a person to be defined as having the metabolic syndrome they must have:

Central obesity (defined as waist circumference* with ethnicity specific values) plus any two of the following four factors:

- **raised TG level**: 150 mg/dL (1.7 mmol/L), or specific treatment for this lipid abnormality
- **reduced HDL cholesterol**: < 40 mg/dL (1.03 mmol/L) in males and < 50 mg/dL (1.29 mmol/L) in females, or specific treatment for this lipid abnormality
- **raised blood pressure**: systolic BP 130 or diastolic BP 85 mm Hg, or treatment of previously diagnosed hypertension
- **raised fasting plasma glucose (FPG)** 100 mg/dL (5.6 mmol/L), or previously diagnosed type 2 diabetes (If above 5.6 mmol/L or 100 mg/dL, OGTT is strongly recommended but is not necessary to define presence of the syndrome).

* If BMI is >30kg/m², central obesity can be assumed and waist circumference does not need to be measured.

NCEP

The US National Cholesterol Education Program Adult Treatment Panel III (2001) requires at least three of the following(6)

- central obesity: waist circumference ≥ 102 cm or 40 inches (male), ≥ 88 cm or 36 inches(female)
- dyslipidemia: TG ≥ 1.7 mmol/L (150 mg/dl)
- dyslipidemia: HDL-C < 40 mg/dL (male), < 50 mg/dL (female)
- blood pressure ≥ 130/85 mmHg
- fasting plasma glucose ≥ 6.1 mmol/L (110 mg/dl)

American Heart Association/Updated NCEP

There is confusion as to whether AHA/NHLBI intended to create another set of guidelines or simply update the NCEP ATP III definition. According to Scott Grundy, University of Texas Southwestern Medical School, Dallas, Texas, the intent was just to update the NCEP ATP III definition and not create a new definition (7, 8):

- Elevated waist circumference:
    - Men — Equal to or greater than 40 inches (102 cm)
    - Women — Equal to or greater than 35 inches (88 cm)

- Elevated triglycerides: Equal to or greater than 150 mg/dL (1.7 mmol/L)
- Reduced HDL ("good") cholesterol:
    - Men — Less than 40 mg/dL (1.03 mmol/L)
    - Women — Less than 50 mg/dL (1.29 mmol/L)
- Elevated blood pressure: Equal to or greater than 130/85 mm Hg or use of medication for hypertension
- Elevated fasting glucose: Equal to or greater than 100 mg/dL (5.6 mmol/L) or use of medication for hyperglycemia

WHO Criteria - the World Health Organization bases it's definition on presence of insulin resistance plus two of the following:

- Insulin resistance :

  Impaired fasting blood glucose (the American Diabetes Association considers the cutoff to be 100 mg/dL) Impaired glucose tolerance (blood glucose above 140 two hours after a 75g glucose challenge) A diagnosis of Type 2 diabetes is automatically included

- High blood pressure (>=140 mm Hg systolic or >=90 mm Hg diastolic) or taking blood pressure medication

- Plasma triglycerides >=150 mg/dL (>=1.7 mmol/L)
- HDL cholesterol <35 mg/dL (<0.9 mmol/L) in men or <39 mg/dL (1.0 mmol/L) in women
- BMI greater than 30 and/or waist:hip ratio >0.9 in men, >0.85 in women
- Urinary albumin excretion rate >=20 μg/min or albumin:creatinine ratio >=30 mg/g

Relationship among metabolic syndrome components

Overweight and increased plasma insulin are key components of the metabolic syndrome(11,12) Bao et al(12) studied > 1,500 individuals in the Bogalusa Heart Study initially when they were 5-23 years of age and then again 8 years later. They found that subjects with consistently high insulin levels had 36 times more overweight, 2.5 times more hypertension,3 times more dyslipidemia than those with low insulin levels. Other studies also support a link among obesity, hyperinsulinemia, and other metabolic syndrome components in youth(9,10,13)

Not only are overweight and hyperinsulinemia associated, but the two factors are also related to dyslipidemia, especially low HDL cholesterol and high triglyceride levels(9,14,15,16). In several studies, overweight youth had higher serum insulin (with normal glucose), higher

triglycerides and blood pressure, and lower HDL cholesterol than non overweight subjects(9,10).

Hypertension is recognized as an important component of the metabolic syndrome in adults, but its role in the syndrome in children and adolescents is not clear. Few studies of youth have examined the relationship of blood pressure and insulin values, and their results are conflicting. Some investigators found a positive association between insulin levels and blood pressure(14,17,18)where as others have not(19,20)

Overweight children had low HDL cholesterol and high triglycerides and insulin, but normal glucose levels(9,10)suggesting that glucose intolerance may develop later than other syndrome abnormalities. Thus, it may be important to assess insulin levels as well as glucose in children, because many with the cluster of metabolic syndrome factors will have normal glucose levels.

The mechanism responsible for the development of insulin resistance in children and adolescents is not well understood. In adults, the mechanism defect associated with insulin resistance occurs on several levels: 1) pre-receptor defect (defective insulin production), 2) receptor defect (decreased or defective receptor sites), 3) glucose transport defect

(abnormal GLUT4 molecules), or 4) post-receptor defect (abnormal signal transduction) (Granberry & Fonseca, 1999). Abnormalities of the insulin molecule are extremely rare. A decreased number of receptor sites as well as defects in post-receptor signaling are more frequently seen in individuals with insulin resistance. Defects in post-receptor signaling often are found in individuals with central obesity and a sedentary lifestyle - two known risk factors for many of the disorders associated with Insulin resistance syndrome (Granberry & Fonseca, 1999). Evidence now exists that these mechanical defects occur in children as well by as early as 6-10 years of age (Uwaifo et al., 2002).

Hypertension

The relation between hypertension and insulin resistance is confounded by the significant independent relation between hypertension and obesity. Hypertension is an integral component of the MetS(21) Increased sympathetic tone has been associated with obesity in adolescents, and both insulin and leptin(22) appear to have a direct effect on sympathetic nervous system activity(23). Insulin infusions stimulate sodium retention by the kidney, and insulin stimulates vascular smooth muscle growth. Fasting insulin, used as an estimate of insulin resistance, has been significantly correlated with blood pressure in

children and adolescents(24). The Cardiovascular Risk in Young Finns study showed a significant correlation between fasting insulin and blood pressure in children and adolescents and also showed that the level of fasting insulin predicted the level of blood pressure 6 years later. Similarly, leptin has direct central effects that increase sympathetic outflow to the kidney. It has been hypothesized that selective leptin resistance maintains leptin-induced sympathetic activation in obesity, which permits leptin to play an important role in the pathogenesis of obesity-related hypertension and MetS. Studies in 11- to 15-year-olds showed a lack of significant correlations for blood pressure with fasting insulin (adjusted for BMI), insulin resistance (measured with the euglycemic clamp), triglycerides, HDL-C, and low-density lipoprotein (LDL) cholesterol. However, when the MetS factors (triglycerides, HDL-C, fasting insulin, and BMI) were considered together as a cluster and comparisons made between children with high and low blood pressure, the cluster score was significantly higher in the high blood pressure group. Thus, despite the lack of a significant relation between blood pressure and the individual risk factors, its relation with the cluster of risk factors is consistent with a clinical association of blood pressure and the MetS before adulthood. Most recently, the Fels

Longitudinal Study showed a strong association between childhood hypertension and adult MetS(25).

Lipid Abnormalities

Lipid abnormalities, particularly high triglycerides and low HDL-C, are strongly associated with insulin resistance(26) and are criteria for the MetS. Studies in rats have shown that hyperinsulinemia stimulates the synthesis of fatty acids by increasing the transcription of genes for lipogenic enzymes in the liver. Fatty acids in turn stimulate increased production of very-low-density lipoprotein. It is currently unknown whether insulin resistance induces dyslipidemia or whether insulin resistance and dyslipidemia are associated via an underlying cause.

Abnormal lipid profiles also are found in children with obesity and insulin resistance (27,28). Data from the Bogalusa Heart Study have shown that overweight children have significantly higher levels of total cholesterol, LDL cholesterol, and triglycerides and lower HDL-C levels than normal-weight children (29). The hypertriglyceridemic waist phenotype has been proposed in adults as a predictor of the MetS. A recent study in more than 3000 adolescents that used the modified ATP III cut points for serum triglycerides (≥110 mg/dL) and waist circumference (≥90th percentile for age and sex) has shown that the

concomitant presence of these criteria was significantly associated with a clustering of metabolic abnormalities, which is characteristic of the MetS

Apo lipoprotein CIII, a marker of the triglyceride-rich lipoproteins increased in MetS, retards triglyceride clearance. This may explain why there is a preponderance of small, dense LDL particles in the setting of MetS along with hypertriglyceridemia. Small, dense LDL particles may have increased atherogenic potential, and the mechanisms proposed for this association are their low affinity to LDL receptors, propensity to undergo oxidative stress, prolonged plasma half-life, and high penetration of the intima. In adults and more recently in children, a high prevalence of small, dense LDL particles was demonstrated in association with abdominal obesity, visceral fat, and insulin resistance. Hypertriglyceridemia is less frequent in blacks, which complicates the determination of appropriate cutoffs for the diagnosis of Mets(30). Independent of weight and insulin status, blacks have lower apolipoprotein CIII levels than other racial subgroups. Accordingly, lower apolipoprotein CIII levels in blacks correlate with less hepatic lipase degradation of triglyceride-rich precursors and less production of small, dense LDL. And yet, LDL lipoprotein sizing still correlates with triglyceride levels in blacks, just in a different range. These findings suggest that perhaps different lipid thresholds should be used for blacks,

because their lower incidence of dyslipidemia, as currently defined, does not lower their risk for T2DM(31) or cardiovascular morbidity(32).

Glucose Intolerance: T2DM

Diabetes mellitus, a metabolic disease characterized by hyperglycemia, is associated with accelerated development of vascular disease. Because insulin is the only significant hypoglycemic hormone, hyperglycemia is the result of either impaired secretion of insulin (type 1), resistance to the effect of insulin in liver or muscle (type 2), or a combination of these pathophysiological situations.

The progression from insulin resistance and impaired carbohydrate metabolism to T2DM has been documented in adults and children (33,34) In adults, weight loss has been shown to reverse this progression, with frank diabetes regressing to insulin resistance. Patients with impaired fasting glucose or impaired glucose tolerance are referred to as "prediabetic," which acknowledges the relatively high risk for development of frank diabetes(35) With the current obesity epidemic and its metabolic consequences, the identification of children with impaired fasting glucose, that is, fasting glucose 100 to 126 mg/dL , is very important, because appropriate management may decrease the progression to T2DM.

Nevertheless, not all children with impaired carbohydrate metabolism develop T2DM. In a study of children with impaired glucose tolerance followed up over a period of 1 year, one third became euglycemic, one third developed T2DM, and one third maintained impaired glucose tolerance (36) Data from the Third National Health and Nutrition Examination Survey (NHANES III) reveal that the prevalence of type 1 diabetes mellitus in adolescents is 1.7/1000, whereas the prevalence of T2DM is 4.1/1000. This increase coincides with increasing rates of overweight and physical inactivity in children (37).

Mechanism:

The mechanisms underlying the metabolic syndrome are not fully known; however resistance to insulin stimulated glucose uptake seems to modify biochemical responses in a way that predisposes to metabolic risk factors. A central role has been attributed to the pro-inflammatory cytokines, tumor necrosis factor a (TNF- a) and interleukin (IL)-6, supported by the fact that both are produced in substantial amounts by human adipose tissue. TNF- a impairs insulin-stimulated glucose uptake in a variety of cells and decreases lipoprotein lipase activity. Both cytokines increase hepatic lipogensis and elicit a systemic acute- phase response. Furthermore, various aspects of the acute-phase response, such

as fibrinogen and plasminogen activator inhibitor-1 levels, whole-blood viscosity, and white blood cell count, have recently been found to correlate positively with the metabolic syndrome. This is of particular interest because inflammation plays an important role in the pathogenesis of atherothrombosis.(38,39)

Macrophage and T-cell infiltration is a major feature of atherosclerotic plaques, especially at sites of plaque rupture, and epidemiological studies show strong positive associations of systemic markers of inflammation with atherothrombotic disease(40,41) Moreover, C-reactive protein (CRP), the classic and exquisitively sensitive acute phase reactant, shows a strong independent association with the risk of Coronary Heart Disease and other atherothrombotic events. CRP levels have also been found to correlate with BMI and some features of the metabolic syndrome.

The AHA/NHLBI/ADA conference identified three potential etiologic categories:

1. Obesity and disorder of adipose tissue.
2. Insulin-resistance
3. A constellation of independent risk factors (e.g. molecules of hepatic, vascular and immunologic origin) that mediate specific

component of syndrome like hypertension, prothrombotic state, lipoprotein metabolic ageing and physical inactivity. Metabolically, several risk factors tend to cluster in middle-aged adults, including HDL-C, BMI, systolic pressure, TGs, glucose and cholesterol. Risk factors occur in isolation only 30% of the time, and clustering of three or more factors occurs 17% of the time in both genders. Clustering of the factors was related to baseline obesity and weight gain during adulthood. Loss of weight over a 16-year period was highly related to a reduced tendency toward clustering of risk factors. In addition, clusters of risk factors were related to greater risk of CHD over the follow up period, and the presence of 3 or more metabolic risk factors led to a doubling of risk for CHD in men and a five-fold increase in risk for women. In Framingham and in other observational studies, the central core of metabolic risk factors were found to be highly related, including triglycerides, HDL-C, BMI, waist circumference, or fasting insulin levels, to insulin levels after an oral glucose challenge test. In addition to a central metabolic syndrome core, there has been a hypertension cluster with shared variance components that included BMI, systolic pressure and diastolic pressure (42) **Risk factors for metabolic syndrome**

Heredity

Children of parents with metabolic syndrome(MetS) and increased cardiovascular risk may be at especially high risk of developing MetS and greater levels of cardiovascular risk factors themselves because of shared genetic and environmental factors(43,44,45) Familial influences on development of cardiovascular risk are well known. Because atherosclerotic cardiovascular disease(ASCVD) - aggregates in families, parental history of ASCVD is accepted as a measure of the offspring's cardiovascular risk and has been used in prevention and intervention algorithms. The Bogalusa Heart Study has shown that offspring of parents with early coronary artery disease were overweight beginning in childhood and developed an adverse cardiovascular risk profile (elevated total cholesterol, LDL cholesterol, and plasma glucose)46 In addition, children and young adults with a parental history of premature ASCVD had higher blood pressure, serum lipids, and homocysteine than those with a negative parental history. Twin and family studies have found substantial familial aggregation for the MetS risk factors(43,44,45)Measures of preclinical atherosclerosis such as c-IMT and functional brachial artery flow-mediated vasodilation showed evidence of early adverse changes in children of parents with premature ASCVD. Conversely, most obese

children have at least 1 parent who is obese, and the risk of adult obesity among children <10 years old is more than doubled if a parent is obese. The familial nature of insulin action in Pima Indians has been known for many years. Relatives of diabetic patients tend to have higher insulin levels than relatives of nondiabetic individuals. A positive family history of T2DM was associated with higher levels of insulin resistance (insulin clamp studies) in 10-year-old black children (47)In a study of 357 children and 378 parents (221 mothers and 157 fathers), children who had at least 1 parent with the MetS (defined by ATP III criteria) had significantly higher levels of obesity, particularly central obesity, and insulin resistance than children in whom neither parent had the MetS.

Lifestyle Behaviors

Television-Watching Habits

Epidemiological studies provide evidence that sedentary behavior, such as television watching, is positively associated with overweight among children and adults(48,49,50) although it is unknown whether watching television contributes to the development of insulin resistance and inflammation. In a recent study conducted among parents and their children enrolled in the Minnesota Heart Survey,

children who watched at least 1 hour of television per day and had 1 or 2 overweight parents were at 15% or 32%, respectively, greater risk of being overweight than children with normal weight parents(51). Furthermore, for each hour of television watched per day, the likelihood of a child being overweight increased 2%; overweight parents watched more television than normal-weight parents.

Physical-Activity

Physical activity is beneficial for weight management and prevention of overweight and obesity in adults and children. There is evidence for an association between physical activity and lower levels of inflammatory cytokines and markers of oxidative stress. Higher levels of physical activity are also positively correlated with insulin sensitivity in adolescents(52) and with improved endothelial function and HDL-C, even in the absence of weight loss. However, most of these data are cross-sectional, and few studies have directly assessed the effect of exercise training on these variables. Many of the controlled intervention studies addressing this issue have shown that exercise improves adipokine and oxidative stress levels; however, most of these trials have reported concomitant improvements in body weight or composition that occurred during the exercise training period. Because

adipocytes are the main mediators of these hormones, changes in body weight/composition confound the data with regard to the direct effects of exercise on these variables. Three studies have recently challenged the notion that exercise directly stimulates improvements in adipokines and inflammatory markers in adults and children(53) independent of weight loss.

Dietary Intake

Increased consumption of whole grain foods decreases the development of coronary heart disease and diabetes and improves insulin sensitivity and inflammation in adults. In a recent study among adolescent boys and girls, greater insulin sensitivity was observed with higher intake of whole grain after adjustment for age, sex, race, Tanner stage, energy intake, and BMI. The same relation was noted among the overweight and obese adolescents(54), as well as in adults. A significant inverse association between fiber intake and the MetS has been described in adults and in the Framingham Offspring Study. Conversely, the prevalence of the MetS is significantly higher among individuals in the highest relative to the lowest quintile category of glycemic index. In 1 study, fiber attenuated the insulin response to ingested carbohydrate, with beneficial effects on

insulin sensitivity, adiposity, and pancreatic function, and it promoted satiety. There is evidence that a diet rich in fruit and vegetables, and therefore, antioxidants and micronutrients in addition to fiber, reduces the risk of ASCVD. Studies in adults have shown inverse relations of inflammatory factors with vitamin C, carotene, magnesium, and long-chain fatty acids. Because we do not eat just 1 nutrient or 1 food, it is important to examine the role of dietary patterns and their relation with health outcomes. Previous studies in adults have shown a Western dietary pattern (a diet high in red and processed meat, fried food, high-fat dairy foods, and sugar-sweetened beverages) to be associated with adverse levels of cardiovascular risk factors, higher BMI, and higher all-cause, ASCVD, and cancer mortality. Conversely, a Mediterranean diet rich in fruits, vegetables, whole grains, and fish, supplemented with olive oil or nuts, has beneficial effects on cardiovascular risk factors Despite these presumed benefits, well-controlled studies in adults and children on the effect of these nutrients on risk for ASCVD are lacking. A recent scientific statement from the American Heart Association provides nutrition recommendations for the promotion of cardiovascular health in children and adolescents and is focused on total caloric intake and eating behaviors as part of a comprehensive healthy lifestyle(55).

Puberty and the metabolic syndrome

Puberty presents a unique challenge to insulin-glucose homeostasis. During puberty, insulin resistance is increased, and insulin sensitivity is reduced in both nondiabetic and diabetic children. This insulin resistance is normally compensated for by increased insulin secretion(56,57,58)Caprio et al(57) suggested that the insulin hypersecretion they found in adolescents may reflect the puberty-associated increase in the amount of circulating growth hormone. Travers et al(59) found that changes in insulin sensitivity during puberty were sex-dependent and suggested that they are related to changes in body composition.

Body fat, blood pressure, and lipids are all affected by puberty. The percentage of body fat increases strikingly in females through adolescence, but changes in body fat in males are not consistent(60) Systolic blood pressure also rises with pubertal stage independent of age, particularly in girls(61,62)Lipids vary by pubertal stage in youth(63,64) For example, total cholesterol drops in mid-puberty and begins rising toward adult levels at the end of puberty(64,65)These lipid changes through puberty complicate the definition of cut-off points for dyslipidemia in youth. In addition, the changes in body fat, blood

pressure, and lipid profiles during puberty may be influenced by the decrease in physical activity and changes in eating habits that are commonly seen during adolescence (66,67).Thus, puberty is a crucial time for the development of the metabolic syndrome, and yet it is a difficult time during which to identify it.

PREVENTION:

General recommendations include decreasing obesity, increasing physical activity, and consuming an anti-atherogenic diet, and have traditionally focused on low total fat intake. A major problem with the focus on low fat is that high-carbohydrate diets can contribute to increasing triglyceride and decreasing high-density lipoprotein (HDL) concentrations. Low-carbohydrate diets have been popular in recent years. However, such diets are typically higher in saturated fat and lower in fruits, vegetables, and whole grains than national dietary recommendations. More recently the quality of carbohydrate has been studied in relation to MetS, including a focus on dietary fiber and glycemic index. Similarly, there has been a move from limiting total fat to a focus on the quality of the fat, with evidence of beneficial effects of replacing some carbohydrate with monounsaturated fat. Other nutrients examined for possible importance include calcium, vitamin D, and

magnesium. Together, the evidence suggests that the components of diet currently recommended as "healthy" are likely also protective against MetS, including low saturated and trans fat (rather than low total fat) and balanced carbohydrate intake rich in dietary fiber, as well as high fruit and vegetable intake (rather than low total carbohydrate); and the inclusion of low-fat dairy foods. Accelerating research on gene-diet interactions is likely to contribute interesting information that may lead to further individualized dietary guidance in the future.

REVIEW OF LITERATURE

REVIEW OF LITERATURE

1. In weiss et al “obesity and the metabolic syndrome in children and adolescents “study done in yale , university school of medicine , with 439 obese children and adolescents beginning in 1999 in the age group of 4 to 20 yrs showed the over all prevelance of metabolic syndrome was 38.7% in moderately obese subjects and 49.7% in severely obese subjects. No overweight or non obese subjects met the criteria for metabolic syndrome .They used national cholesterol education programme (1)adult treatment panel for defining metabolic syndrome. The prevalence increased significantly with increased insulin resistance after adjustment for race or ethnic group and the degree of obesity. C reactive protein levels and adiponectin levels decreased with increased obesity. They followed up 77 subjects after a mean (+/- sd) interval of 21.5 +_ 10.5 months. 16 out of 43 who did not have metabolic syndrome at the time of initial evaluation developed it in follow up. 8 of whom who had impaired glucose tolerance during 1st visit developed type 2 diabetes mellitus during follow up(68)

2. In cook et al -Analyses of cross-sectional data obtained from the Third National Health and Nutrition Examination Survey (1988-1994), which was administered to a representative sample of the

noninstitutionalized civilian population of the United States, the initial sample consisted of 3211 subjects aged 12 to 19 years, to whom the following exclusion criteria were applied: (1) had not fasted for 6 hours, (2) was currently pregnant, or (3) was taking medication classified as a blood glucose regulator, such as insulin, androgens or anabolic steroids, or adrenal corticosteroids. The final sample numbered 2430, including some individuals with 1 or more excluding factors. No children younger than 12 years were instructed to fast as part of NHANES III. criteria for the metabolic syndrome in adults specified by NCEP's ATP III and the adapted definition used in this analysis for adolescents aged 12 to 19 years.

The overall prevalence of the metabolic syndrome in adolescents was 4.2%. It was more common in males (6.1%) than in females (2.1%) and was more frequent in Mexican Americans (5.6%) and whites (4.8%) than black subjects (2.0%). In this sample, 41% of subjects had 1 or more of these risk factors, whereas 14% had 2 or more. There were no subjects who had all 5 of these risk factors. Overall, high triglyceride levels and low HDL cholesterol levels were most common, whereas high fasting glucose levels were the least common. White adolescents had the highest rates of high triglyceride levels (25.5%) and low HDL cholesterol levels (26.1%). Mexican American subjects had the highest rate of abdominal

obesity by waist circumference (13.0%). Black adolescents had the highest proportion of elevated blood pressure (6.2%). Adolescents with the metabolic syndrome had a mean BMI of 30.1 and, on average, were at the 95.5th percentile for BMI by age and sex . Of those adolescents who fulfilled these criteria for the metabolic syndrome, 25.2% were at risk for overweight, by BMI, and 73.9% were overweight(69)

3. Based on Beijing Child and Adolescent Metabolic Syndrome (BCAMS) study with body mass index (BMI), waist circumference (WC) and blood pressure measured, the overweight and obese children were screened among nearly 20 000 children 6-18 years of age in Beijing by Chinese BMI cutoffs for schoolchildren (7-18 years) and the US 2000 CDC Growth Charts--the 85th and 95th percentile (6 years) and were enrolled as the study population. Simultaneously a group of children with normal BMI were selected as the control group and based on the international method of age grouping, each of the above groups was divided further into 4 sub-groups in terms of age: 6-9, 10-12, 13-15 and 16-18 years old, respectively. Fasting plasma glucose (FPG) and insulin (FINS), serum high-density lipoprotein cholesterol (HDL-C) and triglyceride (TG) were examined. HOMA-IR index was calculated for estimating individual insulin resistance. A child who met any three or more of the following five criteria, according to NCEP definition, was

diagnosed as MS. A diagnosis of MS using IDF definition required abdominal obesity plus any two or more of the other four criteria: (1) abnormal obesity: WC > or = P(90); (2) elevated BPs: SBP/DBP > or = P(90); (3) low HDL-C: HDL-C < 1.03 mmol/L (40 mg/dl); (4) high TG: TG > or = 1.24 mmol/L (110 mg/dl); (5) impaired fasting glucose (IFG): FPG > or = 5.6 mmol/L (100 mg/dl).

The prevalence rates of MS by NCEP definition were: 0.9%, 7.6% and 29.8% in the normal weight (control group), overweight and obese children, respectively, which were higher than the rates diagnosed by IDF definition with 0.1%, 5.2% and 28.6% in the three groups. The prevalence rates of individual MS component among obese children were: 81.6% for abnormal obesity, 47.7% for elevated BPs, 35.6% for high TG, 16.9% for low HDL-C, and 13.4% for IFG. Elevated BPs (29.8%), abnormal obesity (27.4%) and high TG (26.0%) were the leading three abnormalities among overweight children. With the increase of BMI, the clustering of MS components and insulin resistance (HOMA-IR) were remarkably increased. HOMA-IR significantly increased as the number of MS component increased(70)

4. In the cross sectional study done in turkey by semiz serap et al from From the Departments of Pediatric Endocrinology Pamukkale University School of Medicine, Denizli, Turkey.

86 obese children (97 females and 89 males), aged 11.2 ± 2.8 (6-16) years and 98 healthy children (46 females and 52 males), aged 10.9 ± 3.2 (6-16) years were recruited for the study, as study and control groups, respectively. Methods: Subjects were evaluated for anthropometry, blood pressure (BP) and biochemical cardiovascular risk factors. Metabolic syndrome was defined in presence of 3 of the following: (i) fasting triglyceride 100 mg/dL; (ii) high density lipoprotein – cholesterol < 50 mg/dL, except in boys aged 15 to 19 years, in whom the cut-off point was 45 mg/dL; (iii) fasting glucose 110 mg/dL; (iv) waist circumference > 75th percentile for age and gender and (v) systolic BP > 90th percentile.

Hypertension, hyperinsulinemia, hyper-cholesterolemia, hypertriglyceridemia, low HDL-C, and high LDL-C frequencies of the obese children were significantly higher than those of control group in both sexes. Elevated systolic and diastolic blood pressures were detected in 17.7% and 15.1% of obese children, respectively. Hyperinsulinemia was shown in 52.2%. There was no subject with diabetes mellitus. Impaired glucose tolerance was found only in 1 (0.5%) subject. 11.3% of

the obese children had high TC, 25.8% had high TG, 36.6% had low HDL-C, and 3.7% had high LDL-C.

The prevalence of metabolic syndrome was 2.1% in obese children. We detected that 79.0% of the obese children had one, two or more risk factors; the rest (20.9%) were free from any risk factor. These frequencies were much lower in the control group. The clustering of one, two and three risk factors was very rare - 12.2%, 7.1% and 0%, respectively(71)

5. **Margoth Caceres et al** studied 61 obese children and adolescents aged between 5 and 18 years old. All children underwent an oral glucose tolerance test and fasting blood sample was also obtained to measure insulin, HDL, LDL and triglycerides serum level. The diagnosis of metabolic syndrome was defined according to National Cholesterol Education Program-Adult Treatment Panel (NCEP-ATP III) criteria adapted for children.

Metabolic syndrome was found in 36% of the children, with a higher rate among males (40%) than females (32.2%) ($p = 0.599$). The prevalence of each of the components was 8.2% in impaired glucose tolerance, 42.6% for high triglyceride level, 55.7% for low levels of high-density lipoprotein cholesterol, and 24.5% for high blood pressure. Insulin resistance (HOMA-IR > 3.5) was found in 39.4% of the children,

with a higher rate in males (50%) than females (29%). A strong correlation was found between insulin resistance and high blood pressure ($p = 0.0148$) and high triglycerides ($p = 0.002$). No statistical significance was found between the presence of acanthosis nigricans and insulin resistance. Acanthosis nigricans was found in (70%) of patients resistant to insulin, but it was also present in 54% of patients sensitive to insulin ($p = 0.14$)(72)

6. de Ferranti, et al . defined pediatric MetS using criteria analogous to ATP III as ≥3 of the following: (1) fasting triglycerides ≥1.1 mmol/L (100 mg/dL); (2) HDL <1.3 mmol/L (50 mg/dL), except in boys aged 15 to 19 years, in whom the cutpoint was <1.2 mmol/L (45 mg/dL); (3) fasting glucose ≥6.1 mmol/L (110 mg/dL); (4) waist circumference >75th percentile for age and gender; and (5) systolic blood pressure >90th percentile for gender, age, and height. MetS prevalence in US adolescents was estimated with the Third National Health and Nutritional Survey 1988 to 1994. Among 1960 children aged ≥12 years who fasted ≥8 hours, two thirds had at least 1 metabolic abnormality, and nearly 1 in 10 had MetS. The racial/ethnic distribution was similar to adults: Mexican-Americans, followed by non-Hispanic whites, had a greater prevalence of MetS compared with non-Hispanic blacks (12.9%, [95% CI 10.4% to 15.4%]; 10.9%, [95% CI 8.4% to 13.4%]; and 2.5%, [95% CI 1.3% to

3.7%], respectively). Nearly one third (31.2% [95% CI 28.3% to 34.1%]) of overweight/obese adolescents had MetS(73)

7.In Mohamed et al study of 932 adolescents, aged 10–19 years, who had complete data and returned for reassessment 3.6 years later were investigated. Prevalence of metabolic syndrome according to the ATP III at baseline was 7.4% (95% CI 5.7–9) and after 3.6 years of follow-up was 6.7% (5–8) .There was a significant association between metabolic syndrome prevalence (according to ATP III criteria) and BMI, as 57.9% of overweight adolescents had the metabolic syndrome compared with 29.2% of adolescents at risk for overweight and 2.4% of adolescents with normal weight ($P < 0.0001$). High fasting triglycerides and low HDL cholesterol were the most prevalent components according to ATP III criteria (38.4 and 41.6%, respectively), whereas high fasting blood glucose (FBG) was the least common (1%). Lowering the FBG cut point from 110 to 100 mg/dl increased the percentage of subjects who met this standard from 1 to 7.6%, and lowering waist circumference cut point from the 90th percentile to the 75th percentile for sex and age increased the proportion of subjects who met this standard from 10.3 to 27.3%.Overweight adolescents were 5.69 times as likely to develop metabolic syndrome (95% CI 2.31–13.96). Subjects with waist circumference more than the 90th percentile for age and sex had 2.24

times more chance to develop metabolic syndrome (95% CI 1.01–4.97). On logistic regression, no significant association was seen between FBG, triglycerides, HDL cholesterol, blood pressure, and age with metabolic syndrome incidence(74)

8. In Martha rodriguez -Morán, study, they determined the prevalence of the metabolic syndrome among children and adolescents aged 10–18 years from northern Mexico and evaluate a definition for its early diagnosis in the young population.

Data were analyzed for 965 children and adolescents (51.7% female), who had an average age of 13.0 ± 2.6 years and BMI of 23.5 ± 5.8 kg/m^2. The prevalence of family history of diabetes, hypertension, and obesity was 43.6% (95% CI 40.5–46.8), 40.9% (37.8–44.1), and 29.4% (26.6–32.5), respectively, and the prevalence of obesity, elevated blood pressure, hyperglycemia, hypertriglyceridemia, and low HDL cholesterol was 27.7% (24.8–30.5), 7.1% (5.5–8.8), 7.7% (6.0–9.4), 9.5% (7.7–11.4), and 20.8% (18.3–23.4), respectively. Diagnosis of type 2 diabetes and hypertension was established in 17 (1.8%; 95% CI 1.0–2.8) and 13 (1.4%; 0.8–2.4) participants.

Prevalence of the metabolic syndrome, according to the Adult Treatment Panel III, AACE, World Health Organization, EGIR, and

REGODCI definitions was 6.5% (95% CI 4.7–7.8), 7.7% (6.0–9.4), 4.5% (3.2–5.8), 3.8% (2.6–5.1), and 7.8% (6.1–9.5), respectively.

A total of 697 (72.2%) subjects were lean; among them at least one family phenotype, one clinical trait, or one abnormal laboratory criterion was identified in 43.8, 21.3, and 20.6%. Sixty-one (8.7%) lean subjects fulfilled the REGODCI criterion for laboratory test, establishing diagnosis of the metabolic syndrome in 13 (21.3%; 95% CI 11.8–33.7) of them. On the other hand, diagnosis of the metabolic syndrome was established in 70 (26.1%; 21.0–31.5) obese children. The number of children and adolescents who were diagnosed with the metabolic syndrome was significantly lower according to the EGIR definition, whereas the AACE and REGODCI definitions identified the highest prevalence (75)

9. Atabek ME have studied 169 obese children and adolescents (body mass index>95th percentile), 100 prepubertal and 69 pubertal, aged between 7 and 18 years. Each subject was submitted to an oral glucose tolerance test. The diagnosis of impaired glucose tolerance, type 2 diabetes and metabolic syndrome were defined according to modified WHO criteria adapted for children.

Metabolic syndrome was found in 27.2%, with a significantly higher rate among adolescents aged 12-18 years (37.6%) than among children aged 7-11 years (20%) ($p < 0.001$). There were no significant differences in the prevalence of metabolic syndrome by sex. The prevalences of insulin resistance, glucose intolerance and type 2 diabetes were 29, 19 and 2% among prepubertal children and 56.5, 27.5 and 4.3% among pubertal group, respectively. The prevalence of fasting hyperinsulinemia in pubertal group was significantly higher than prepubertal children ($p < 0.001$). Hyperinsulinemia was also more frequent in pubertal children with significant difference (20% versus 43.7%, $p < 0.001$). Hypertension was significantly more common in adolescents (31.8%) than children (15%) with obesity, as expected ($p < 0.013$). Overall, dyslipidaemia in prepubertal and pubertal groups was identified in 42 and 55%, respectively, with no significant differences ($p = 0.085$)(76)

10. In another study by Calcaterra where they studied 191 obese [body mass index (BMI) > 97th percentile] children and adolescents. Obesity was stratified on the basis of a threshold BMI z-score and subjects were classified as moderately (z-score 2–2·5) or severely obese (z-score > 2·5). Seventy-six, nonobese subjects were recruited into a

comparison group. Thirty-one of them were of normal weight (BMI < 75th percentile) and 45 overweight (BMI 75th–97th percentile).

Patients were classified as having MS if they met three or more of the following criteria for age and sex: BMI > 97th percentile, triglyceride levels > 95th percentile, high density lipoprotein (HDL) cholesterol level < 5th percentile, systolic or diastolic blood pressure > 95th percentile and impaired glucose tolerance (blood glucose level: 7·8–11·1 mmol/l at 2 h). Insulin resistance was calculated using the homeostasis model assessment for insulin resistance (HOMA-IR) and impaired insulin sensitivity was defined as a HOMA-IR ≥ 2·5 in prepubertal patients and HOMA-IR > 4 in pubertal subjects.

The overall prevalence of MS was 13·9% and was present in 12·0% of moderately obese and 31·1% of severely obese subjects; no overweight or normal weight subjects met the criteria for MS. The rate of the MS increased progressively with increasing BMI categories (P < 0·001).Severely obese patients had a threefold increased risk with respect to moderately obese patients(77)

11.Prevalence of the Metabolic Syndrome in Iranian Adolescents[*] by Ahmad Esmaillzadeh[*] et al The prevalence of the metabolic syndrome was 10.1% (95% confidence interval: 9.0 to 11.1) among Iranian

adolescents (boys: 10.3% , 8.6 to 11.8; girls: 9.9% , 8.4 to 11.3). Overall, low serum high-density lipoprotein-cholesterol and high serum triglycerides were the most common components of the metabolic syndrome (42.8% and 37.5% , respectively). Overweight subjects had the highest proportion of metabolic syndrome compared with those at risk for overweight and those with normal weight (boys: 41.1% vs. 11.4% and 3.0% , respectively, $p < 0.01$; girls: 43% vs. 15.2% and 5.0% , respectively, $p < 0.01$).

12. Metabolic Syndrome in Overweight and Obese Japanese Children by Masao Yoshinaga et al showed Japanese obese children to have a significantly lower prevalence (17.7%) of the metabolic syndrome than U.S. obese adolescents (28.7%, $p = 0.0014$). However, Japanese overweight children had a similar incidence (8.7%) of the metabolic syndrome compared with U.S. overweight adolescents (6.8%). Hyperinsulinemia in girls and abdominal obesity in boys are characteristic features of individual metabolic syndrome factors in Japanese children.

13. Ethnic differences in metabolic syndrome among overweight and obese children and adolescents: the Oslo Adiposity Intervention Study.

Two hundred and three overweight and obese Norwegian, Pakistani, Tamil and Turkish patients aged 6-17 years living in Norway were included. Metabolic syndrome was defined as the presence of at least three abnormal values of waist circumference, blood pressure, fasting triglycerides, fasting glucose and HDL cholesterol. The prevalence of metabolic syndrome was significantly higher among the immigrant compared to Norwegian subjects when adjusted for age, gender and BMI-Z-score (20.8 vs. 30.6%; OR = 2.2, 95% CI = 1.05-4.77). The prevalence of metabolic syndrome increased with increasing severity of obesity and reached 50% in severely obese immigrants and 30% in severely obese Norwegians. Among the overweight subjects metabolic syndrome prevalence was 23.5% among immigrants and 19.4% among Norwegians.

STUDY JUSTIFICATION

STUDY JUSTIFICATION

Childhood obesity is considered to be a disease of epidemic proportion. Metabolic syndrome is increasing in prevalence with rising childhood obesity and sedentary lifestyles. Children with metabolic syndrome frequently progress to type 2 DM and have increase risk for mortality and morbidity from cardiovascular diseases. Hence there is a vital need for early identification of children with this syndrome and modification of risk factors to prevent further progression.

AIMS AND OBJECTIVES

AIMS AND OBJECTIVES

- To estimate the prevalence of metabolic syndrome among 7-18yrs old overweight and obese children.
- Second objective was to determine the association between insulin resistance and components of metabolic syndrome.

MATERIALS AND METHODS

MATERIALS AND METHODS

METHODOLOGY

Study design

Descriptive study

Study period:

October 2008 to September 2010

Study place:

Endocrine department of Institute of child health and hospital for children,

Egmore, Chennai, 3 government and private schools.

INCLUSION CRITERIA:

Children in the age group 7 – 18 yrs who satisfy the criteria for obese with the BMI on CDC chart more than 95th centile

EXCLUSION CRITERIA:

- presence of diabetes

- use of drugs that alters blood pressure or glucose or lipid metabolism
- syndromic obesity
- endocrinological disorder

Consent:

Instituitional consent was obtained from the parents after explaining the nature of the study.

MANOEUVRE:

This cross sectional study was done in endocrinology department of children's hospital egmore .children attending our OPD are screened for obesity with BMI, and those who satisfy the inclusion criteria were enrolled in the study after informing the nature of the study to the parents. Written informed consent was obtained from parents or guardians of obese patients children who were offered the study. 82 children were enrolled of which 35 were female and 47 were male. The same investigator performed anthropometric measurements and complete physical examination including pubertal staging, neurological, mental and dysmorphic findings. Obese subjects were included in study after the exclusion of any with endocrinological disorders or obesity syndromes. Tanner classification was used for pubertal staging.

Information about the level of physical activity was recorded using a self-reporting questionnaire, including level of daily activities, time spent indoors watching TV, using computers, playing computer and video games, and studying. Birth weight, pattern of nutrition, duration of breast feeding and obesity, and age at onset of obesity were also assessed.

Family history of obesity, DM, hypertension (HT), cerebrovascular events, coronary artery disease, dyslipidemia (DL), gestational diabetes in the first and second degree relatives, and educational status of the parents were recorded.

Anthropometry: Body weight was measured to the nearest 0.1 kg with a balance scale , and height was measured to the nearest 0.1 cm with stadiometer with subjects lightly dressed and without shoes. Body mass index (BMI) was calculated as weight (kg) divided by height square (m2).

The mercury sphygmomanometer has always been regarded as the gold standard for clinical methods. The Korotkoff technique is used for measuring blood pressure_Traditionally, the sounds have been classified as 5 phases: phase I, appearance of clear tapping sounds corresponding to the appearance of a palpable pulse; phase II, sounds become softer and longer; phase III, sounds become crisper and louder; phase IV, sounds become muffled and softer; and phase V,

sounds disappear completely. the onset of phase I corresponds to systolic pressure The disappearance of sounds (phase V) corresponds to diastolic pressure

Since number of factors related to the subject can cause significant deviations in measured blood pressure like room temperature, exercise, positioning of the arm, muscle tension, bladder distension, talking, and background noise, the children are asked to remove all clothing that covers the location of cuff placement and comfortably seated, with the legs uncrossed, and the back and arm supported, such that the middle of the cuff on the upper arm is at the level of the right atrium (the mid-point of the sternum and are instructed to relax as much as possible and to not talk during the measurement procedure; ideally, 5 minutes before the first reading is taken. cuff is deflated at the rate of 2 to 3 mm Hg per second. A minimum of 2 readings are taken at intervals of at least 1 minute, and the average of those readings are used to represent the patient's blood pressure. If there is >5 mm Hg difference between the first and second readings, additional (1 or 2) readings are obtained, and then the average of these multiple readings is used. Values more than 90^{th} centile for age and sex considered high.

Laboratory investigations: Blood glucose, serum insulin and lipid levels were determined from blood samples taken after an overnight fast.

Biochemical analysis and definition:

Hyperinsulinemia is defined if fasting insulin >15mu/L, HOMA IR > 3.5

HOMA IR is calculated as product of fasting plasma insulin in mu/L and the fasting glucose in mg/dl, divided by 405.Score of >3.5 is taken as insulin resistance and score < 3.5 as insulin sensitive. Fasting glucose >110mg/dl is considered abnormal and >140mg/dl is taken as having Diabetes mellitus

Triglycerides >100mg/dl, HDL < 40 mg/dl is considered cut off.

Metabolic syndrome was considered if three or more of the following criteria were present: BMI > 95^{th} percentile, triglyceride >40mg/dl, HDL <40mg/dl, fasting glucose >110mg/dl, systolic or diastolic BP >90^{th} percentile.

Statistical analysis:

All statistical analysis (mean, median, standard deviation) was done using SSPS version 11 for windows. Fisher's exact test was used to determine statistical differences in presence of metabolic syndrome

criteria according to sex and to correlate the association among insulin resistance presence or absence and metabolic syndrome criteria plus acanthosis nigricans. T test was calculated to determine statistical significance ($p < 0.05$) in clinical and biochemical characteristics according to sex.

OBSERVATION

OBSERVATION

Sex distribution of study population

TABLE 1

Male	47 (57.31)
female	35(42.68)

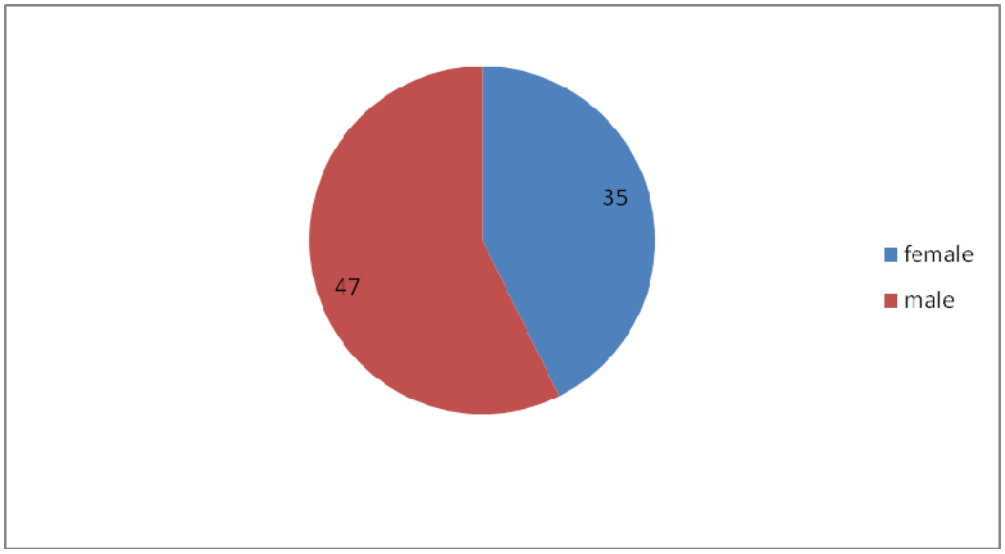


TABLE 2

Clinical characteristics according to sex

characteristics	Male (N=47) Mean ± SD	Female(N=35) Mean ± SD	P VALUE *
Age (yrs)	11.57±2.78	10.3± 2.90	0.6
Wt(kg)	54.10±14.16	55.72± 13.90	0.11
Ht(cms)	141.7±12.9	138.6± 13..2	0.105
BMI	26.33±2.39	25.58± 2.33	0.3
Systolic BP	109.8± 13.2	107.4±12.88	0.43

*T test is used to calculate p value

This table depicts the clinical characteristics of male and female. No significant difference observed between the sex for height, weight ,BMI, blood pressure. Youngest female 7.2 yrs eldest 17yrs, male - youngest 7yrs and eldest 17.8 yrs. Highest BMI in female is 30.2 against 30.3 in male.

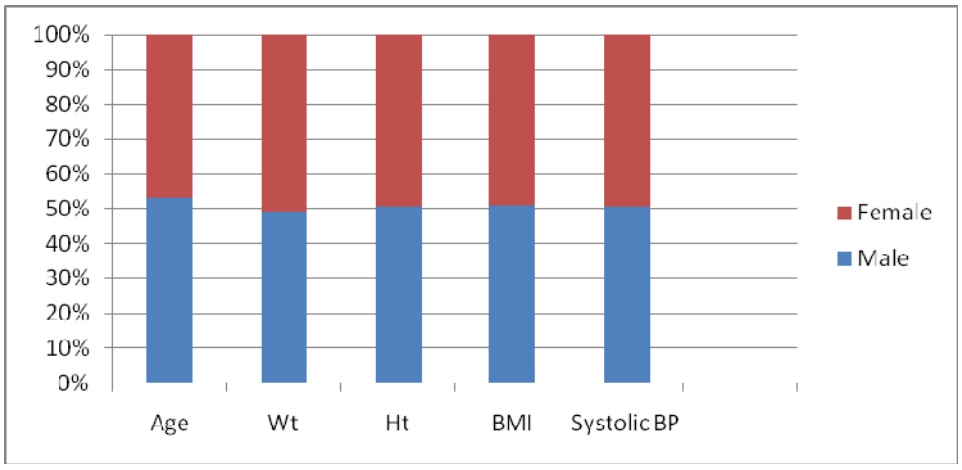


Table 3

Biochemical characteristics according to sex

Characteristics	Male(N=47) Mean ± SD	Female(N=35) Mean ±SD	P Value *
HDL (mg/dl)	42.03±6.73	40.95± 6.83	0.3
LDL (mg/dl)	116.3± 15.35	118.11± 15.3	0.29
TGL(mg/dl)	99.04± 11.45	99.15±11.09	0.96
Cholesterol(mg/dl)	158.8± 19.13	157.13± 19.97	0.23
Fasting glucose(mg/dl)	89.28± 13.96	90.45± 13.81	0.326
Fasting insulin(mu/L)	15.44± 4.56	16.79± 4.39	0.16
HOMA IR	3.44± 1.19	3.71± 1.21	0.28

*t test is used to calculate p value

HDL-high density lipoprotein, LDL- low density lipoprotein,

TGL-triglycerides, IR- insulin resistance

In this table showing the biochemical characteristics no significant p value in obtained for any criteria . HDL range 26 to 78mg/dl, LDL range from 36 to 154mg/dl, TGL 31 to 159mg/dl, total cholesterol 49 to 214 mg/dl, fasting glucose 59 to 148 mg/dl, fasting insulin 5 to 25.8 mu/l ,HOMA IR range from 2 to 7.1.

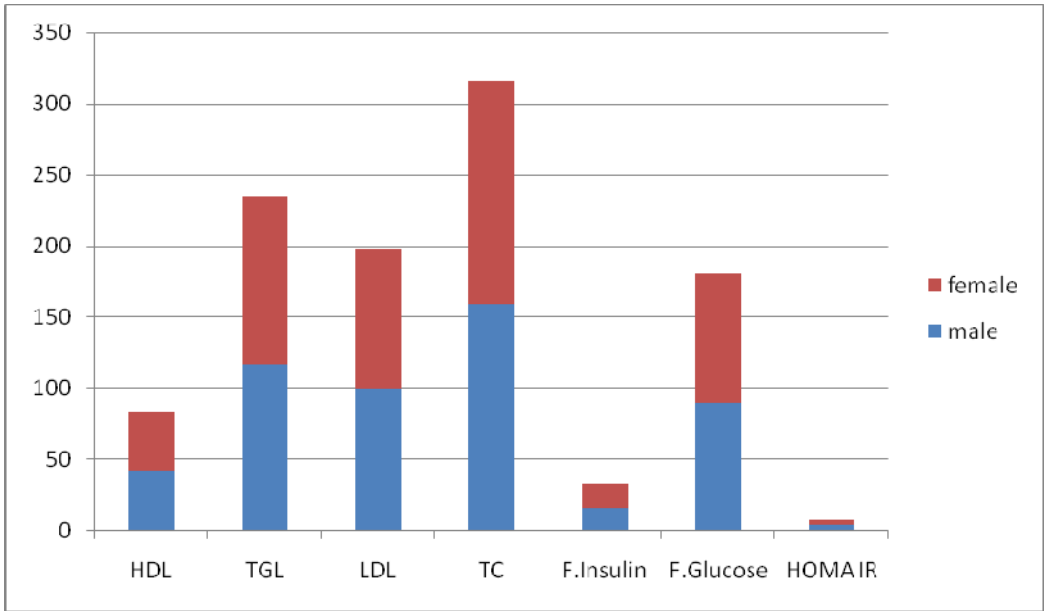


Table 4

Metabolic profile and metabolic syndrome criteria according to sex.

Characteristics	Male N (%)	Female N (%)	Total N (%)	P Value*
BMI	47(100)	35(100)	82(100)	-
IGT	1(2.1)	2(5.7)	3(3.6)	0.572
DM	-	1 (2.8)	1(1.1)	0.426
Sys BP	15(31.9)	9(25.7)	24(29.2)	0.805
HDL	12(25.5)	12(34.2)	24(29.2)	0.464
TGL	16(34)	13(37.1)	29(35.3)	0.818
HOMA IR	12(25.5)	13(37.1)	25(30.4)	0.333
MS	13(27.6)	8(22.8)	21(25.6)	0.798

A.NIGRICANS	11(23.4)	13(37.1)	24(29.2)	0.222

*fisher t test is used to calculate p value

IGT-impaired glucose tolerance, DM-diabetes mellitus, sys BP- systolic blood pressure, MS- metabolic syndrome.

The metabolic parameters does not vary with sex and there is no significant difference in any parameter between the groups. Of the 3 children with impaired fasting glucose level 1 had diabetes mellitus. 21 persons had features of metabolic syndrome of which 13 are male 8 are female.

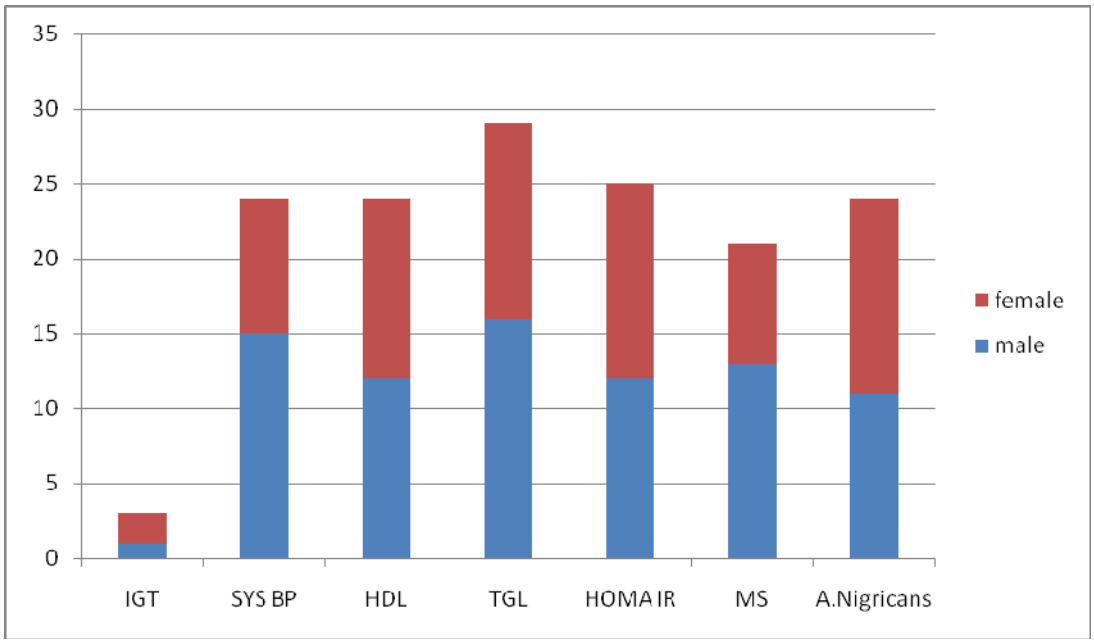


Table 5

Prevalence of component of metabolic syndrome according to insulin resistance

characteristics	Insulin resistance N=25 N (%)	Insulin sensitive N=57 N (%)	P Value *
IGT	3(12)	0	0.02
Sys BP >95th	12(48)	12(21)	0.186
HDL	10(40)	14(24.5)	0.19
TGL	14(54)	15(26.3)	0.012
A.Nigricans	11(44)	13(22.8)	0.06

*fisher t test is used to calculate p value

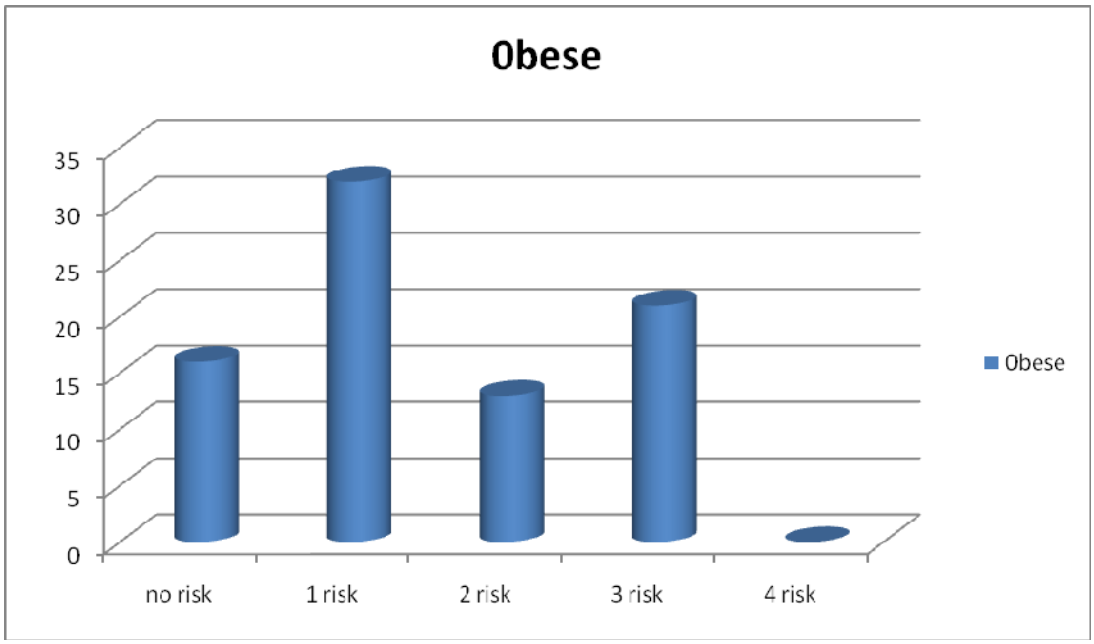
Insulin resistance is significantly associated with impaired glucose tolerance and elevated triglycerides and acanthosis nigricans. Although persons with insulin resistance have higher prevalence of blood pressure and abnormal HDL levels they are not statistically significant.

Table 6

Clustering of risk factors in the obese and non obese children

characteristics	Obese (N=82)	Percentage
No risk factors	16	19.5
1 risk factor	32	39
2 rick factors	13	15.8
3 risk factors	21	25.6
4 risk factors	0	-

Out of the 82 obese children almost one fourth of them has metabolic syndrome and 39% has atleast one risk factor for cardiovascular disease followed in order with children having no risk factors and then last with 2 risk factors. None of the 82 children had all 4 risk factors


Obese
35
30
25
20
15
10
5
0
no risk
1 risk
2 risk
3 risk
4 risk
Obese

DISCUSSION

DISCUSSION

The prevalence of metabolic syndrome is reported to be 30–50% among obese children [*14*, *43*]. There has been a tremendous increase in the number of studies on obesity and MS in children; however, there are conflicting results [*6*, *31*]. This is mainly due to the lack of consensus on the diagnostic criteria of MS in children and adolescents. In addition to the previous attempts, there is now greater consensus regarding the components of MS during childhood and adolescence. These should include central obesity, insulin resistance, glucose intolerance, hypertension, and dyslipidemia [*48*]. However, this new definition using age-specific cutoffs has not yet resolved the issue completely, and it is suggested that MS should not be diagnosed in children younger than 10 years [*48*].

The prevalence of the metabolic syndrome varies by the definitions used for the components and by the weight status of the subjects. Cook et al.,[6] who studied children and adolescents 12-19 years of age in the third National Health and Nutrition Examination Survey (NHANES III) data set, reported a prevalence of 4.2%. Investigators from the Bogalusa Heart Study[25] reported a prevalence of 3.6% in youth 8-17 years of age. However, researchers reported much higher prevalence rates in children

who are overweight or obese.[6,7] In a study of 490 subjects aged 4-20 years, 89% of whom had a BMI ≥ 97th percentile, the prevalence of the metabolic syndrome in moderately obese subjects (defined as a BMI *z*-score of 2.0-2.5) was 38.7%, whereas almost half (49.7%) of severely obese subjects (defined as a BMI *z*-score > 2.5) had the syndrome.[7] In another study among children and adolescents 8-19 years of age, the prevalence was 6.8% in those who were at risk for overweight (85-95th percentile of BMI) and 28.7% in those who were overweight (BMI ≥ 95th percentile).[8]

The prevalence of the metabolic syndrome in youth may vary by sex and ethnicity, as it does in adults, but data on this are conflicting. In a national multiethnic study, the metabolic syndrome was significantly more prevalent in males (6.1%) than in females (2.1%),[6] but other researchers reported no significant sex differences.[8] Cook et al.[6] reported the prevalence of the metabolic syndrome was higher in whites (4.8%) and Mexican Americans (5.6%) than in African Americans (2.0%). Weiss et al.[7] also found that white children were at greater risk for metabolic syndrome than were African-American children when they used the same cut points for lipids. However, when they used race-specific norms for lipids, the prevalence of the metabolic syndrome risk did not differ between African-American and white youth, likely because the African-

American youth had better lipid profiles. More large, multiethnic studies with boys and girls are needed to learn whether the ethnic and sex differences seen in the metabolic syndrome in adults are also present during childhood and adolescence.

The prevalence of metabolic syndrome in obese children in this study conducted in children's hospital is 25.6 % which is similar to the prevalence of metabolic syndrome in Hispanic youth study by Martha et al. This result suggests that MS has become a serious problem in our country. In the literature, there are diverse statements on the impact of gender and puberty on the prevalence of MS [*4*, *16*, *17*, *41*]. Cook et al. [*14*], Cruz et al. [*16*], and Weiss et al. [*43*] reported a higher prevalence of MS and its components in male compared to female children. In this study no such sex difference was noticed.

The prevalence of hypertension and dyslipidemia in the form of elevated triglycerides and low HDL are 29.2%, 29.2% and35.3% respectively. Only 3.6% had impaired glucose concentration of which 1 had frank diabetes mellitus. In a study by Viner et al. [*41*], the prevalence of dyslipidemia, HT, IGT, and elevated fasting insulin were 30%, 32%, 11%, and 0.8%, respectively, while type 2 DM was not observed in any patient [*41*]. This is almost comparable to this study. The prevalence of

IGT and type 2 DM in European obese children and adolescents were 7.5% and 1.2%, respectively [*45*]. In Italy, the corresponding prevalences were 4.5%, and 0.1%, respectively [*24*]. The prevalence of type 2 DM in Germany (1.5%) was higher than that in Sweden (0.5%), with the prevalence of IGT (20–25%) and type 2 DM (4%) being highest in the US [*36*, *42*, *46*].

The prevalence of CV risk factors in obese children can change because of varying diagnostic criteria and cut-off values used in different studies [*16*, *17*]. According to Viner et al.'s study [*41*], the prevalence of the presence of two risk factors in obese children, aged 2–18 years, was 36%, while the prevalence of patients with three and four risk factors were 28% and 5%, respectively. In another study done in turkey by yasar sen , the prevalence of children with two CV risk factors was 37.5%, while with three and four risk factors were found to be 31.5% and 10.3%, respectively. In our study the results are 31.7% with 1 risk factor and 28% , 25.6% with 2 and 3 risk factors respectively similar to those of the study by Viner et al. [*41*].

Impaired glucose tolerance was more common in persons with insulin resistance than in persons with insulin sensitivity as shown by significant p value. Similarly hypertriglyceridemia was significantly

associated with insulin resistance. Other parameters like HDL abnormality or hypertension was not observed to have significant relation with insulin resistance when individual components were considered.

Our study provides evidence showing a high prevalence of the metabolic syndrome in obese adolescents and children. Further study could better show the pathophysiology of metabolic syndrome in adolescents and its relationship to other chronic diseases.

SUMMARY AND CONCLUSION

SUMMARY AND CONCLUSION

- In this study the prevalence of metabolic syndrome in obese children is 25.6%.
- The percentage of obese children with hypertension, elevated triglycerides and low high density cholesterol are 29.2%, 29.2%, 35.3% respectively.
- 3.6% has impaired glucose tolerance, and 1 child has frank type 2 diabetes mellitus.
- This high prevalence of metabolic syndrome signifies the need for early screening of obese children for components of metabolic syndrome.

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ANNEXURE

ANNEXURE

PROFORMA

REG NO:

NAME:

AGE/SEX:

ADDRESS:

Age of onset of obesity:

Onset:

Progression:

Hours of television watching

Per day: per week:

Hours of exercise

Per day: per week:

Frequency of eating junk foods:

SYMPTOMS OF HYPOTHYROIDISM:

Lethargy

Cold intolerance

Constipation

Poor school performance

Neck swelling

FAMILY H/O

Obesity

Diabetes

Hypertension

Coronary artery disease

History of drug intake:

EXAMINATION:

Height:

BMI:

Weight:

Blood pressure: 1ST 2ND Mean BP:

Pulse rate:

Waist circumference:

Acanthosis nigricans :

Neck swelling:

Dry skin:

INVESTIGATIONS:

Fasting glucose:

Fasting triglycerides:

Fasting HDL:

Fasting LDL:

Fasting serum insulin:

HOMA IR:

Thyroid function test: